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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/535,500	05/26/2006	Anne Mette Buhl Hertz	55320.001041	7327

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EXAMINER	
GUSSOW, ANNE	
ART UNIT	PAPER NUMBER
1643	

MAIL DATE	DELIVERY MODE
05/05/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/535,500	HERTZ ET AL.	
	Examiner	Art Unit	
	ANNE M. GUSSOW	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 April 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *43-48,50-57 and 61-66* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *43-48,50-57 and 61-66* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The previous office action mailed March 30, 2009 is hereby withdrawn in view of applicant's re-filing of the non-compliant supplemental amendment on April 9, 2009.

2. Claims 1-42, 49, and 58-60 have been cancelled.

Claims 43-45, 50-53, 55-57, and 62 have been amended.

3. Claims 43-48, 50-57 and 61-66 are under examination.

4. The species election between the sequences, as set forth in the Office action mailed on April 23, 2007, has been reconsidered. Claim 48, 51, 52, 55-57, and 65 directed to non-elected sequences are no longer withdrawn from consideration because the sequences are overlapping transcripts in a genomic region that is only transcribed in B-CLL patients with poor prognosis.

In view of the above noted withdrawal of the species election, applicant is advised that if any claim presented in a continuation or divisional application is anticipated by, or includes all the limitations of, a claim that is allowable in the present application, such claim may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application.

Once a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. See *In re Ziegler*, 443 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

5. The following office action contains NEW GROUNDS of Rejection.

Information Disclosure Statement

6. The information disclosure statement (IDS) submitted on December 23, 2008 has been fully considered by the examiner and an initialed copy of the IDS is included with the mailing of this office action.

Rejections Withdrawn

7. The rejection of claims 43-47, 49, 50, 53, and 54 under 35 U.S.C. 112, first paragraph as lacking enablement is withdrawn in view of applicant's declaration and the new grounds of rejection below.

NEW GROUNDS of Rejection

Claim Objections

8. Claim 50 objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 50 is not further

limiting with respect to SEQ ID No. 13 in the base claims because SEQ ID No. 13 represent exon 3 and the sequences in claim 50 are larger transcripts which do not each contain exon 3.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 43-48, 50-57 and 61-66 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for diagnosing a subtype of B-CLL with poor prognosis by detecting mRNA transcripts using primers to detect the exon 2/exon 3 splice junction or using SEQ ID Nos. 13, 15-17 as probes, does not reasonably provide enablement for diagnosing a subtype of B-CLL by detecting SEQ ID Nos. 13 or 15-17. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in In re Wands, 8 USPQ2d 1400 (CAFC 1988).

> Wands states on page 1404,
> "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working

examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The claims are broadly drawn to detecting SEQ ID Nos. 13 and 15-17 in patients having a poor prognosis of B-CLL. The specification discloses SEQ ID Nos. 13 and 15-17 as being exons 1-3 and a coding sequence respectively. The sequences represent DNA regions of the larger genomic sequence SEQ ID Nos. 1 and 5. The specification discloses the sequences of SEQ ID Nos. 13 and 15-17 were used as probes in northern blots to detect transcription in this genomic region, i.e., transcripts which "comprise" these exon sequences. The specification does not disclose detection of DNA in diagnosing B-CLL. The specification does not disclose detection of RNA transcripts comprising only SEQ ID Nos. 13 and 15-17.

Buhl, et al. (Blood, 2006. vol. 107, pages 2904-2911, as cited on the IDS filed December 23, 2008) teach detection of transcription products from the CLLU1 region (SEQ ID No. 1) by RT-PCR and northern blots as being indicative of a poor prognosis of B-CLL. Buhl, et al. teach a number of differentially spliced transcripts in this genomic region (see figure 2). Buhl, et al. do not teach detection of DNA being indicative of poor prognosis of B-CLL. Josefsson, et al. (Blood, 2007. Vol. 109, pages 4973-4979, as cited on the IDS filed December 23, 2008) teach RT-PCR detection of transcripts from the CLLU1 region in patients with poor prognosis of B-CLL.

While the shorter exon sequences can be detected, detection of just the exon sequences would not provide a predictable nexus or link between detection and a poor prognosis. The specification discloses isolation of RNA to detect transcripts (example

3). The specification indicates the criticality of the presence of the complete transcripts. The specification discloses the correlation with a poor prognosis of B-CLL and the detection of complete transcripts and the absence of a correlation between the detection of just SEQ ID Nos. 13, 15, 16, or 17 and a correlative poor prognosis (page 36 and figures 3 and 10).

There is insufficient evidence or nexus that would lead the skilled artisan to predict the ability to diagnosis a poor prognosis of B-CLL by detecting SEQ ID Nos. 13 and 15-17. The specification does not teach detection of DNA in determining a poor prognosis of B-CLL. The specification does not teach detection of RNA transcripts consisting of SEQ ID Nos. 13 or 15-17.

In view of the lack of the predictability of the art to which the invention pertains undue experimentation would be required to practice the claimed methods with a reasonable expectation of success, absent a specific and detailed description in applicant's specification of how to effectively practice the claimed methods and absent working examples providing evidence which is reasonably predictive that the claimed methods are effective for diagnosing a poor prognosis of B-CLL, commensurate in scope with the claimed invention.

Conclusion

11. No claims are allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANNE M. GUSSOW whose telephone number is

(571)272-6047. The examiner can normally be reached on Monday - Friday 8:30 am - 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Anne M. Gussow
May 4, 2009

/David J Blanchard/
Primary Examiner, Art Unit 1643